REMARKS

Claims 1-4 and 6-10 were pending at a mailing of the Sep. 26 Non-Final Office Action. Claims 3, 5 and 14 have been cancelled. Claims 1, 4, 6, 8 and 9 are amended. Claim 15 is new. No new matter is introduced. A withdrawal of all rejections is respectfully requested.

Claim Objections

Examiner objects to Claims 1-14 for grammatical errors.

Applicant made the appropriate corrections to claims 1, 3, and 8.

Claim Rejections - 35 U.S.C. §112, second paragraph:

Examiner rejects Claims 1-4 and 6-14 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim subject matter.

Examiner rejects Claim 1 because a relationship between "extracellular DNA" and "blood" isn't defined.

Applicant amends the claim to include the term "in" between the former and the latter.

Examiner rejects Claim 1 because the term "certain" fails to establish metes and bounds.

Applicant deletes the indefinite term from the claim.

Examiner rejects Claim 1 because it is not clear if "gastric" and "colon" cancers are separate alternatives or one specific condition.

Applicant deletes those cancers from the claim to overcome section 112, first paragraph, rejections.

Examiner rejects Claim 1 because the language fails to clearly link the patient population to which the treatment agent is administered.

Applicant disagrees. Applicant is uncertain what language Examiner requires and respectfully requests that Examiner more clearly define the requirement. Applicant amends the claim to clarify that patients diagnosed with at least one of the cancers or diseases listed in the preamble are administered the agent in their blood stream.

Examiner rejects Claim 1 stating that the terms "destroying agent" and "destroyed DNA" are not defined in the specification.

Applicant contends that a "destroying agent" is defined in the Jun. 24, 2008 amended "Summary of the Invention" section as an agent that destructs, modifies, or binds blood's extracellular DNA to slow down malignant cancer growth. This agent is more specifically defined in the specification as one that alters the electrophoretic profile of extracellular DNA. The term "destroyed DNA" is defined in the specification to be the extracellular DNA in cancer patients that is destructed, modified, or bound by the destroying agent. The "destroyed DNA" is more specifically extracellular DNA with altered electrophoretic profiles.

Examiner rejects Claim 4 because "uninterrupted" was not clearly defined.

Applicant amends into the claim the "doses" limitation which is supported in the specification and included in the amended "Summary " submitted with the Jun. 24, 2008 reply.

Examiner rejects Claim 9 because "term of life" is not clearly defined.

Applicant amends the claim to include a clarifying limitation: a term of treatment is from diagnosis for a remain life.

Claim Rejections - 35 U.S.C. §112, first paragraph:

Examiner rejects Claims 1-4 and 6-14 under 35 U.S.C. § 112, first paragraph, because the specification is only enabling for Erlich carcinoma, lung carcinoma, and malignant and low differentiated lymphoma.

Applicant argues that Claim 1 is within the bounds for enablement of treating those specific diseases listed in the specification. Applicant contends that a pilot study has shown successful for the cancers listed in the preamble of the present claim. Pilot clinical trials of DNASE enzyme monotherapy in patients with advanced cancer of different origin were performed in St.Petersburg Academy of Advanced Medical Education; Department of Thorax Surgery. 'A total of 12 patients were included according to following inclusion criteria:

- Men and women 18 y. or older
- T4M+ advanced cancer of any origin
- Diagnosis proved by clinical, instrumental and laboratory assessment
- Absence of any alternative treatment modality
- CT (Spiral Computer Tomography) or clinical evidence of rapidly progressing disease
- Karnofsky performance score >40

The following patients were included:

- MOI - Malignant Melanoma. Multiple lung and liver metastasis.
- GEF- Breast cancer. Disseminated bone metastasis.
- FVV-Breast cancer. Disseminated lung and liver metastasis.
- KNP- Gastric cancer. Disseminated lymphatic and liver metastasis.
- PGP-Colon cancer. Disseminated lung and liver metastasis.
- MCF-Colon cancer. Local relapse. Disseminated lymphatic and liver metastasis.
- MVI-Pancreatic adenocarcinoma. Disseminated lymphatic metastasis.
- SSA- Lung cancer. Disseminated lung and lymphatic metastasis.

- ISP- Colon cancer. Liver metastasis.
- BVI- Recurrent Renal cancer. Multiply bone metastasis.
- CLV- Recurrent rectal carcinoma. Multiply bone and lung metastasis.
- BAI- Lung cancer. Disseminated lung and lymphatic metastasis

The patients received one course of monotherapy with bovine pancreatic DNASE enzyme according following treatment schedule:

- Treatment duration -21 day.
- DNASE delivery-20 min. intravenous infusion in isotonic sodium chloride.
- Number of daily infusions - 6.
- Day 1-8: 50 mg per infusion (510 000 Kunitz units per day)
- Day 8-12: 75 mg per infusion (765 000 Kunitz units per day)
- Day 12-21: 100 mg per infusion (1 020 000 Kunitz units per day)

The efficacy was assessed on day 30 after initiation of therapy. All patients demonstrated stabilization of the disease assessed by spiral CT scan according RECIST criteria. All patients demonstrated significant increase in Karnofsky performance score; some patients show shrinkage of metastatic nodules. So, DNASE therapy is effective in treatment of malignant tumors of different origin.

Examiner rejects Claims 1-4 and 6-14 under 35 U.S.C. § 112, first paragraph, because the scope of diseases to be treated was not supported in the original filed specification.

Applicant contends that lung carcinoma is specifically supported in the specification in Example 3 (Pg. 3, line 4 to Pg. 16, line 10), and malignant lymphoma is specifically supported in the specification in Example 4 (Pg. 16, line 11 to Pg. 17, line 19).

Claim Rejections - 35 USC § 102:

Claims 1 and 3 are rejected under 35 U.S.C. §102(b) as being anticipated by Young (WO 01/74905).

Applicant essentially claims in Ind. Claim 1a method to treat lung carcinoma, Erlich carcinoma, and lymphoma, whercin a DNAse enzyme is introduced in a circulating blood stream to destroy extracellular DNA. Young teaches a method/compound to treat epithelial cancers (s.a., ovarian, gastric, colorectal, and pancreatic), wherein a DNAse compound is transfected into a CHO L761h cell(s), in the ovary cell line. Young's method/compound targets and destroys dysfunction populations of cells expressing PEM.

Young constructed the chimerical protein which ultimately contains a target-cell specific portion that is specifically designed to deliver chimerical protein inside specific cells. Such chimera goes inside a specific PEM portion of targeted cells in few minutes after intravenous injection; hence, the Young invention *destroys intracellular* DNA similar to other anti-cancer remedies. Young more specifically states the following:

> By "target cell specific" portion we mean the portion of the compound which comprises one or more binding sites which recognize and bind to polymorphic epithelial mucin (PEM) on the target cell. Upon contact with the target cell, the target cell specific portion is preferably internalized along with the cytotoxic portion. Such internalization results in the cytotoxic portion being delivered to the cell cytosol, where it has access to the cell's nucleic acid molecules.

There is no possibility that such chimera will bound and cleave extracellular DNA particularly due to the lack of a DNA-binding portion and preservation of only the catalytically active portion in the DNA structure.

The fundamental distinction between Young's and Applicant's invention is that the latter destroys extracellular DNA.

Claims 1 and 3 are rejected under 35 U.S.C. §102(b) as being anticipated by Sugihara, *et al.*

(*Br. J. Cancer*, 1993, 67, 66-70).

Applicant claims a method of certain cancer and disease treatments which targets DNA circulating in blood which originated from tumoral or mutant cells. The method includes the steps of fractionally administering DNase solution into a patient. Sugihara limits its teaching to theory, in which it simply supposes that DNase I can prevent blood-borne metastasis. This theory is advanced by the influence of DNase I on tumor cell arrest; however, there is no teaching as to treatment method. Applicant contends that just because the author theorizes that DNase I would be effective, he does not indicate that the method includes steps of acting on or inactivating extracellular DNA circulating in blood plasma; rather, Sugihara limits its method to the following steps: (1) DNase treatment in the microvasculature of the liver, or (2) removing primary tumor mass and DNase treatment. There is no discussion in the abstract about extracellular DNA targets circulating in blood plasma.

Sugihara wrote DNase treatment does not affect primary tumor growth and that Dnase treatment is not satisfactory. The Sugihara author did not recognize or understand the role of inactivation of free circulating extracellular DNA in cancer treatment. An absence of that knowledge results in an improper usage of DNase and an ineffective treatment. It is widely accepted in pharmacology arts that only knowledge or proper pharmacological targets results in effective treatment. A skilled physician, knowing the necessity to destroy free circulating extracellular DNA, or knowing the desired pharmacodynamic criteria, could provide effective dosage regimes that result in effective treatment.

Sugihara studied chemotrypsine and desoxiribonuclease I (DNase I) enzymes that influence autologic and heterologic adhesion of tumor cells during their metastasing. Sugihara shows that systematic introduction of Dnase I could slow metastasis development. The effect Sugihara finds is therapeutically insufficient. Its authors conclude that DNase I can be used altogether with surgical elimination of tumors for prevention of tumor cells' hematogenic dissemination. The authors mean the influence of DNase I to be on tumor cells' *cytoplasmatic membrane* and *not* on

destruction of *circulating DNA*. Accordingly, the regime and doses that were used could not decrease circulating DNA levels.

Sugihara teaches a dose of 0.1 Kunitz Units per mouse per day, while the present specification taught 1 666 Kunitz Unit per mouse per day. This amount is 16,000 times more, which is critical for extracellular DNA destruction since extracellular DNA is 1000 times more resistant to DNase enzyme rather than conventional plasmid or intracellular DNA. Sugihara failed to recognize the need and the method to destroy extracellular DNA, and it thus never disclosed a use of DNase in proper doses.

Applicant adds new claim 15 which includes this dose limitation.

Claim Rejections - 35 USC § 103:

Claims 1-4, 6 and 9 are rejected under 35 U.S.C. §103(a) as being obvious over Young.

Examiner is directed to Applicant's foregoing argument made specifically against the Young reference on pages 8 and 9 (against the section 102 rejection) of this reply.

Claims 1-4, 6 and 9 are rejected under 35 U.S.C. §103(a) as being obvious over Sugihara.

Examiner is directed to Applicant's foregoing argument made specifically against the Sugihara reference on pages 9 and 10 (against the section 102 rejection) of this reply.

Claims 7 and 8 are rejected under 35 U.S.C. §103(a) as being obvious over Sugihara and Young and further in view of Shak, *et al.* (*Proc. Nat'l Acad. Sci.*. 1990, 87, 9188-9192).

Examiner is directed to Applicant's foregoing arguments made specifically against the Young and Sugihara references on pages 8-10 (against the section 102 rejection) of this reply. Applicant contends that this combination is improper because both of the primary references of the combination fail to teach all limitations in the Independent Claim 1; more specifically, both

references fail to teach a treatment that destroys extracellular DNA. The Young reference teaches a treatment that destroys intracellular DNA. Sugihara teaches destruction of the cytoplasmatic membrane and not destruction of circulating DNA. The present rejected dependent claims incorporate limitations of the Independent Claims. Shak alone fails to teach the limitations of the base claims, and the combination too fails to disclose all limitations; hence, these claims are allowable for at least the reasons set forth for their base claim.

Claims 12 and 13 are rejected under 35 U.S.C. §103(a) as being obvious over Sugihara and Young and further in view of Leland, *et al.* (*Chem. & Bio.*, 2001, 8, 405-13).

Examiner is directed to Applicant's foregoing arguments made specifically against the Young and Sugihara references on pages 8-10 (against the section 102 rejection) of this reply. Applicant contends that this combination is improper because both of the primary references of the combination fail to teach all limitations in the Independent Claim 1; more specifically, both references fail to teach a treatment that destroys extracellular DNA. The Young reference teaches a treatment that destroys intracellular DNA. Sugihara teaches destruction of the cytoplasmatic membrane and not destruction of circulating DNA. The present rejected dependent claims incorporate limitations of the Independent Claims. Leland alone fails to teach the limitations of the base claims, and the combination too fails to disclose all limitations; hence, these claims are allowable for at least the reasons set forth for their base claim.

Claim 14 is rejected under 35 U.S.C. §103(a) as being obvious over Sugihara and Young and further in view of Leland and further in view of Nestle & Roberts (*J. Biol. Chem.*, 1969, 244, 5213-5218).

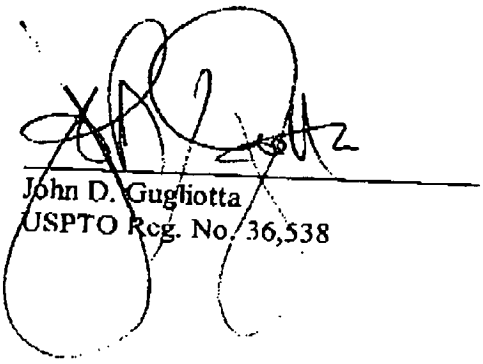
Examiner is directed to Applicant's foregoing arguments made specifically against the Young and Sugihara references on pages 8-10 (against the section 102 rejection) of this reply. Applicant contends that this combination is improper because both of the primary references of the combination fail to teach all limitations in the Independent Claim 1; more specifically, both

references fail to teach a treatment that destroys extracellular DNA. The Young refcrence teaches a treatment that destroys intracellular DNA. Sugihara teaches destruction of the cytoplasmatic membrane and not destruction of circulating DNA. The present rejected dependent claims incorporate limitations of the Independent Claims. Nestle & Roberts alone fails to teach the limitations of the base claims, and the combination too fails to disclose all limitations; hence, these claims are allowable for at least the reasons set forth for their base claim.

CONCLUSION

In view of the amendments submitted herein and the above comments, it is believed that all the grounds of rejection are overcome and that the application has now been placed in full condition for allowance. Should there be any further questions, Examiner is urged to telephone Applicant's undersigned attorney at (330) 253-2225

Respectfully Submitted,



John D. Gugliotta
USPTO Reg. No. 36,538

PC&T Law Group, LLC
Interlake Corporate Center
4199 Kinross Lakes Parkway, Suite 275
Richfield, OH 44286
Ph: (330) 253-2225
Fax: (330) 659-5855
johng@inventorshelp.com